

AMENDMENTS TO THE CLAIMS

Please amend claims 76, 78 and 92 and please cancel claims 77, 81-83, 90 and 91 without prejudice or disclaimer and please add claims 93-100. The following listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-75 (Cancelled)

76. (Currently Amended) A peptide, which is a sequence variant and a functional and/or structural mimic of peptide YY, said peptide comprising ~~at least one modification of the amino acid sequence set forth in SEQ ID NO: 20 (h-PYY 3-36), wherein said peptide~~
- ~~includes a modification that conformationally constrains the relative position of the N-terminal amino acid of that part of SEQ ID NO 2 present in the peptide and amino acid 34 of SEQ ID NO: 2 in the peptide; and/or~~
- ~~includes a branched amino acid sequence resulting in 2 free N-terminal amino acids; and/or~~
- ~~includes N-terminal and/or C-terminal addition of a net basic amino acid sequence;~~
- ~~optionally further includes deletion of amino acids 1-5 of SEQ ID NO: 2; and/or~~
- ~~includes deletion of any one or more of amino acid residues 8-15 of SEQ ID NO: 2 without deletion of all of amino acids 1-7 of SEQ ID NO 2; and/or~~
- ~~includes deletion of amino acids 6 and 7 of SEQ ID NO: 2 without deletion of all of amino acids 1-5 of SEQ ID NO 2; and/or~~
- ~~includes deletion of amino acids 16-19 of SEQ ID NO: 2 without deletion of all of amino acids 1-15 of SEQ ID NO 2; and/or~~
- ~~includes two cross linkable protected Cys amino acid substitutions; wherein said peptide further comprises at most 6 substitutions in the amino acid sequence~~

~~set forth in SEQ ID NO: 2, each of which is a structure and/or functionality preserving substitution.~~

77. (Cancelled)

78. (Currently Amended) A peptide of formula I

$R^1-X-Y-Z-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}$ SEQ ID NO:
20-R²

(I)

wherein

~~A²² is Ala or a structure and/or functionality preserving substitution thereof;~~

~~A²³ is Ser or a structure and/or functionality preserving substitution thereof;~~

~~A²⁴ is Leu or a structure and/or functionality preserving substitution thereof, His or Cys;~~

~~A²⁵ is Arg or a structure and/or functionality preserving substitution thereof;~~

~~A²⁶ is Leu or a structure and/or functionality preserving substitution thereof, His or Cys;~~

~~A²⁷ is Tyr or a structure and/or functionality preserving substitution thereof;~~

~~A²⁸ is Leu or a structure and/or functionality preserving substitution thereof, or Cys;~~

~~A²⁹ is Asn or a structure and/or functionality preserving substitution thereof; or Lys, which is optionally coupled to an amino acid sequence via a peptide bond at the c-amino group;~~

~~A³⁰ is Leu or a structure and/or functionality preserving substitution thereof;~~

~~A³¹ is Val or a structure and/or functionality preserving substitution thereof, or Cys;~~

~~A³² is Thr or a structure and/or functionality preserving substitution thereof;~~

~~A³³ is Arg or a structure and/or functionality preserving substitution thereof;~~

~~A³⁴ is Gln or a structure and/or functionality preserving substitution thereof;~~

~~A³⁵ is Arg or a structure and/or functionality preserving substitution thereof; and~~

~~A³⁶ is Tyr or a structure and/or functionality preserving substitution thereof;~~

~~Z is a peptide of formula~~

~~A¹³-A¹⁴-A¹⁵-A¹⁶-A¹⁷-A¹⁸-A¹⁹-A²⁰-A²¹~~

~~which is absent or wherein,~~

~~A¹³ is Ser or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁴ is Pro or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁵ is Glu or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁶ is Glu or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁷ is Leu or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁸ is Asn or a structure and/or functionality preserving substitution thereof;~~

~~A¹⁹ is Arg or a structure and/or functionality preserving substitution thereof;~~

~~A²⁰ is Tyr or a structure and/or functionality preserving substitution thereof; and~~

~~A²¹ is Tyr or a structure and/or functionality preserving substitution thereof;~~

Y is a peptide of formula

~~A⁸-A⁹-A¹⁰-A-B~~

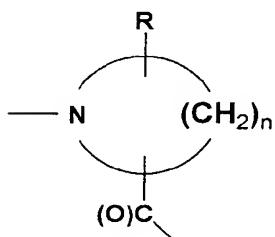
~~which is absent or wherein~~

~~A⁸ is Pro or a structure and/or functionality preserving substitution thereof;~~

~~A⁹ is Gly or a structure and/or functionality preserving substitution thereof;~~

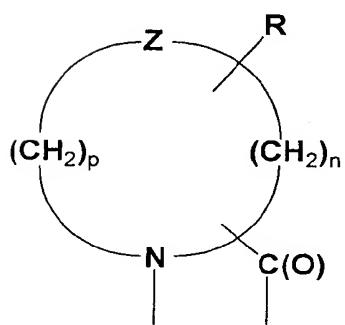
~~A¹⁰ is Glu or a structure and/or functionality preserving substitution thereof, or absent; and~~

A-B designates a dipeptide A¹¹-A¹² selected from the group consisting of Gly-Gly, Pro-Gly, Gly-Pro, Sar-Sar, Sar-Hyp, Hyp-Sar, Pro-Sar, Sar-Pro, Pro-Hyp, Pro-Pro, Hyp-Pro, and Hyp-Hyp, where Pro and Hyp independently may be an L or D form, where the ring structure of Pro (III) and Hyp is optionally substituted with halogen, nitro, methyl, amino, or phenyl, Hyp represents 3-hydroxyproline or 4-hydroxyproline, Sar represents sarcosine, or one or both of the amino acid residues of A-B is a Sar, or an N-cyclohexylglycine residue, or A and B each independently represents a group of the formula II



(IIa)

wherein n is an integer having the value 3, 4, or 5, and R represents an optional substituent, preferably selected from the group consisting of halogen, phenyl, hydroxy, NH₂, and C(1-6)alkyl optionally substituted with halogen, or A-B designates the formula IIa



wherein n is an integer having the value 0, 1, 2, and 3, p is an integer having the value 0, 1, 2, and 3, Z represents O or S, and R represents an optional substituent, preferably selected from the group consisting of halogen, phenyl, hydroxy, NH₂, and C(1-6)alkyl, or A and B independently represents an amino acid residue having a

saturated carbocyclic structure of 4, 5 or 6 members and where in said carbocyclic structure further comprises one or more heteroatoms,

X is a peptide of formula

$A^3-A^4-A^5-A^6-A^7$

which is absent or wherein

A^3 is Ile or a structure and/or functionality preserving substitution thereof, or Cys;

A^4 is Lys or a structure and/or functionality preserving substitution thereof;

A^5 is Pro or a structure and/or functionality preserving substitution thereof, or Cys;

A^6 is Glu or a structure and/or functionality preserving substitution thereof; and

A^7 is Ala or a structure and/or functionality preserving substitution thereof, or Cys;

R^1 is absent or an amino acid sequence;

and

R^2 is absent or an amino acid sequence;

wherein said peptide comprises at most one disulfide bridge selected from $Cys^3-S-S-Cys^{31}$, $Cys^3-S-S-Cys^{28}$, $Cys^5-S-S-Cys^{26}$, and $Cys^7-S-S-CYS^{24}$

or wherein A is absent, Asp or a structure and/or functionality preserving substitution thereof and B is absent, Ala or a structure and/or functionality preserving substitution thereof and said peptide comprises a disulfide bridge selected from $Cys^3-S-S-Cys^{31}$, $Cys^3-S-S-Cys^{28}$, $Cys^5-S-S-Cys^{26}$, and $Cys^7-S-S-Cys^{24}$;

wherein the number of structure and/or functionality preserving substitutions does not exceed 6;

wherein the C-terminal amino exposes a free carboxylic acid group or an amide group;

and

or a multimer and/or pharmaceutically acceptable salt thereof.

79. (Previously Presented) The peptide according to claim 76, which binds with higher affinity to receptor Y2 than to receptor Y1.

80. (Previously Presented) The peptide according to claim 76, which binds with higher affinity to receptor Y5 than to receptor Y1.

Claims 81 - 83 (Cancelled)

84. (Previously Presented) The peptide according to claim 78, comprising the disulfide bridge Cys³-S-S-Cys³¹, or comprising the disulfide bridge Cys³-S-S-Cys²⁸, or comprising the disulfide bridge Cys⁵-S-S-Cys²⁶, or comprising the disulfide bridge Cys⁷-S-S-Cys²⁴.

85. (Previously Presented) The peptide according to claim 78, wherein X has the amino acid sequence set forth in SEQ ID NO: 23 or wherein X is absent.

86. (Previously Presented) The peptide according to claim 78, wherein A and B, independently are selected from the group consisting of N- and C(0)- radicals of the following compounds:

D/L-azetidin-3-carboxylic acid,

D/L-azetidin-2-carboxylic acid,

D/L-Indolin-2-carboxylic acid,

D/L-1,3-dihydro-isoindol-1-carboxylic acid,

D/L-thiazolidin-4-carboxylic acid,

D/L-pipecolinic acid,

D/L-nipecotinic acid,

isonipecotinic acid,

L/D-2-carboxymorpholin,

L/D-1,2,3,4-tetrahydroquinolin-3-carboxylic acid,

L/D-1,2,3,4-tetrahydroquinolin-3-carboxylic acid, and

4-carboxy-4-phenyl-piperidin.

87. (Previously Presented) The peptide according to claim 78, wherein A-B designates 4-(2-aminoethyl)-6-dibenzofuranpropionic acid.
88. (Previously Presented) The peptide according to claim 78, wherein A-B is a dipeptide or wherein A and B both designate Pro or a derivative thereof.
89. (Previously Presented) The peptide according to claim 78, wherein A and B independently represents an amino acid residue having a saturated carbocyclic structure of 4, 5 or 6 members, wherein said carbocyclic structure further comprises one or more heteroatoms selected from the group consisting of N, O and S.
90. (Cancelled)
91. (Cancelled)
92. (Currently Amended) A method for reducing or enhancing body weight in a subject, the method comprising administering, to the subject, an appropriately effective amount of:
- (i) a peptide, which is a sequence variant and a functional and/or structural mimic of peptide YY, said peptide comprising ~~at least one modification of the amino acid sequence set forth in SEQ ID NO: 20 (h-PYY 3-36), wherein said peptide~~
~~includes a modification that conformationally constrains the relative position of the N terminal amino acid of that part of SEQ ID NO 2 present in the peptide and amino acid 34 of SEQ ID NO: 2 in the peptide; and/or~~
~~includes a branched amino acid sequence resulting in 2 free N terminal amino acids; and/or~~
~~includes N terminal and/or C-terminal addition of a net basic amino acid sequence;~~
~~optionally further includes deletion of amino acids 1-5 of SEQ ID NO: 2; and/or~~
~~includes deletion of any one or more of amino acid residues 8-15 of SEQ ID NO: 2 without deletion of all of amino acids 1-7 of SEQ ID NO 2; and/or~~

— includes deletion of amino acids 6 and 7 of SEQ ID NO: 2 without deletion of all of amino acids 1-5 of SEQ ID NO 2; and/or

— includes deletion of amino acids 16-19 of SEQ ID NO: 2 without deletion of all of amino acids 1-15 of SEQ ID NO 2; and/or

— includes two cross linkable protected Cys amino acid substitutions; wherein said peptide further comprises at most 6 substitutions in the amino acid sequence set forth in SEQ ID NO: 2, each of which is a structure and/or functionality preserving substitution; or-of

(ii) a peptide of formula I

$R^1-X-Y-Z-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}$ SEQ ID NO:
20-R²

(I)

Wherein

A^{22} is Ala or a structure and/or functionality preserving substitution thereof;

A^{23} is Ser or a structure and/or functionality preserving substitution thereof;

A^{24} is Leu or a structure and/or functionality preserving substitution thereof, His or Cys;

A^{25} is Arg or a structure and/or functionality preserving substitution thereof;

A^{26} is Leu or a structure and/or functionality preserving substitution thereof, His or Cys;

A^{27} is Tyr or a structure and/or functionality preserving substitution thereof;

A^{28} is Leu or a structure and/or functionality preserving substitution thereof, or Cys;

A^{29} is Asn or a structure and/or functionality preserving substitution thereof, or Lys, which is optionally coupled to an amino acid sequence via a peptide bond at the s-amino group;

A^{30} is Leu or a structure and/or functionality preserving substitution thereof;

~~A³¹ is Val or a structure and/or functionality preserving substitution thereof, or Cys;~~

~~A³² is Thr or a structure and/or functionality preserving substitution thereof;~~

~~A³³ is Arg or a structure and/or functionality preserving substitution thereof;~~

~~A³⁴ is Gln or a structure and/or functionality preserving substitution thereof;~~

~~A³⁵ is Arg or a structure and/or functionality preserving substitution thereof; and~~

~~A³⁶ is Tyr or a structure and/or functionality preserving substitution thereof;~~

~~Z is a peptide of formula~~

~~A¹³-A¹⁴-A¹⁵-A¹⁶-A¹⁷-A¹⁸-A¹⁹-A²⁰-A²¹~~

~~which is absent or wherein,~~

~~A¹³ is Ser or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁴ is Pro or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁵ is Glu or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁶ is Glu or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁷ is Leu or a structure and/or functionality preserving substitution thereof or absent;~~

~~A¹⁸ is Asn or a structure and/or functionality preserving substitution thereof;~~

~~A¹⁹ is Arg or a structure and/or functionality preserving substitution thereof;~~

~~A²⁰ is Tyr or a structure and/or functionality preserving substitution thereof; and~~

~~A²¹ is Tyr or a structure and/or functionality preserving substitution thereof;~~

~~Y is a peptide of formula~~

~~A⁸-A⁹-A¹⁰-A-B~~

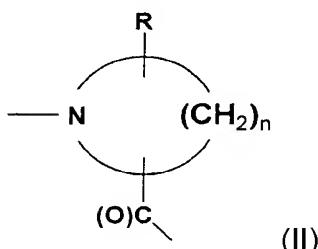
which is absent or wherein

A⁸ is Pro or a structure and/or functionality preserving substitution thereof;

A⁹ is Gly or a structure and/or functionality preserving substitution thereof,

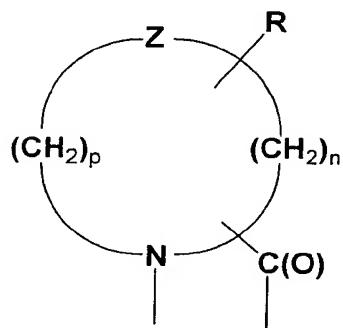
A¹⁰ is Glu or a structure and/or functionality preserving substitution thereof, or absent; and

A-B designates a dipeptide A¹¹-A¹² selected from the group consisting of Gly-Gly, Pro-Gly, Gly-Pro, Sar-Sar, Sar-Hyp, Hyp-Sar, Pro-Sar, Sar-Pro, Pro-Hyp, Pro-Pro, Hyp-Pro, and Hyp-Hyp, where Pro and Hyp independently may be an L or D form, where the ring structure of Pro and Hyp is optionally substituted with halogen, nitro, methyl, amino, or phenyl, Hyp represents 3-hydroxyproline or 4-hydroxyproline, Sar represents sarcosine, or one or both of the amino acid residues of A-B is a Sar, or an N-cyclohexylglycine residue, or A and B each independently represents a group of the formula II



wherein n is an integer having the value 3, 4, or 5, and R represents an optional substituent, preferably selected from the group consisting of halogen, phenyl, hydroxy, NH₂, and C(1-6)alkyl optionally substituted with halogen, or

A-B designates the formula IIa



wherein n is an integer having the value 0, 1, 2, and 3, p is an integer having the value 0, 1, 2, and 3, Z represents O or S, and R represents an optional substituent, preferably selected from the group consisting of halogen, phenyl, hydroxy, NH₂, and C(1-6)alkyl, or A and B independently represents an amino acid residue having a saturated carbocyclic structure of 4, 5 or 6 members and where in said carbocyclic structure further comprises one or more heteroatoms,

X is a peptide of formula

A³-A⁴-A⁵-A⁶-A⁷

which is absent or wherein

A³ is Ile or a structure and/or functionality preserving substitution thereof, or Cys;

A⁴ is Lys or a structure and/or functionality preserving substitution thereof;

A⁵ is Pro or a structure and/or functionality preserving substitution thereof, or Cys;

A⁶ is Glu or a structure and/or functionality preserving substitution thereof; and

A⁷ is Ala or a structure and/or functionality preserving substitution thereof, or Cys;

R¹ is absent or an amino acid sequence; and

R² is absent or an amino acid sequence;

wherein said peptide comprises at most one disulfide bridge selected from Cys³-S-S-Cys³¹, Cys³-S-S-Cys²⁸, Cys⁵-S-S-Cys²⁶, and Cys⁷-S-S-Cys²⁴;

or wherein A is absent, Asp or a structure and/or functionality preserving substitution thereof and B is absent, Ala or a structure and/or functionality

preserving substitution thereof and said peptide comprises a disulfide bridge selected from Cys³-S-S-Cys³¹, Cys³-S-S-Cys²⁸, Cys⁵-S-S-Cys²⁶, and Cys⁷-S-S-Cys²⁴;

wherein the number of structure and/or functionality preserving substitutions does not exceed 6;

wherein the C-terminal amino exposes a free carboxylic acid group or an amide group; and

or a multimer and/or pharmaceutically acceptable salt thereof.

93. (New) The method according to claim 92, wherein the peptide is of formula I and binds with higher affinity to receptor Y2 than to receptor Y1.
94. (New) The method according to claim 92, wherein the peptide is of formula I and binds with higher affinity to receptor Y5 than to receptor Y1.
95. (New) The method according to claim 92, wherein the peptide is of formula I and comprises the disulfide bridge Cys³-S-S-Cys³¹, comprises the disulfide bridge Cys³-S-S-Cys²⁸, or comprises the disulfide bridge Cys⁵-S-S-Cys²⁶, or comprising the disulfide bridge Cys⁷-S-S-Cys²⁴.
96. (New) The method according to claim 92, wherein the peptide is of formula I and wherein X has the amino acid sequence set forth in SEQ ID NO: 23 or wherein X is absent.
97. (New) The method according to claim 92, wherein the peptide is of formula I and wherein A and B, independently are selected from the group consisting of N- and C(0)- radicals of the following compounds:
D/L-azetidin-3-carboxylic acid,
D/L-azetidin-2-carboxylic acid,
D/L-Indolin-2-carboxylic acid,
D/L-1,3-dihydro-isoindol-1-carboxylic acid,
D/L-thiazolidin-4-carboxylic acid,

D/L-pipecolinic acid,
D/L-nipecotinic acid,
isonipecotinic acid,
L/D-2-carboxymorpholin,
L/D-1,2,3,4-tetrahydroquinolin-3-carboxylic acid,
L/D-1,2,3,4-tetrahydroquinolin-3-carboxylic acid, and
4-carboxy-4-phenyl-piperidin.

98. (New) The method according to claim 92, wherein the peptide is of formula I and wherein A-B designates 4-(2-aminoethyl)-6-dibenzofuranpropionic acid.
99. (New) The method according to claim 92, wherein the peptide is of formula I and wherein A-B is a dipeptide or wherein A and B both designate Pro or a derivative thereof.
100. (New) The method according to claim 92, wherein the peptide is of formula I and wherein A and B independently represents an amino acid residue having a saturated carbocyclic structure of 4, 5 or 6 members, wherein said carbocyclic structure further comprises one or more heteroatoms selected from the group consisting of N, O and S.